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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,505	06/28/2001	Saluh Kivlighn	50193-109	4997

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/892,505	KIVLIGHN ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the communication filed on 07/05/2007. Applicant's amendment filed on 07/05/2007, added new claim 18.

Currently, claims 16-18 are pending.

Applicant's arguments have been fully considered, and found persuasive. The rejection of claims 16-17 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is herein withdrawn.

Applicant's arguments have been fully considered, and found persuasive. The rejection of claims 16-17 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is herein withdrawn.

Applicant's arguments have been fully considered, but not found persuasive. The rejection of claim 16 under 35 U.S.C. 103(a) as being unpatentable over Maeda et al. (5,747,495, PTO-892), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892) is MAINTAINED. See under response to arguments.

Applicant's arguments have been fully considered, but not found persuasive. The rejection of claim 16 under 35 U.S.C. 103(a) as being unpatentable over Baldwin et al. (4,032,522, PTO-892), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892) is MAINTAINED. See under response to arguments.

Applicant's arguments have been fully considered, but not found persuasive. The rejection of claims 16-17 under 35 U.S.C. 103(a) as being unpatentable over Nakamoto et al. (EP 0 337 350, PTO-1449), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892) is MAINTAINED. See under response to arguments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maeda et al. (5,747,495, PTO-892), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892).

Maeda et al. discloses a method of treating hypertension comprising administering to a patient in need thereof a therapeutically effective amount of a uric acid lowering agent, a xanthine oxidase inhibitor, 4-amino-6-hydroxypyrazolol [3,4-d]pyrimidine (AHPP). See abstract; column 2, lines 11-13; column 6, Example 9, claim 1. For oral administration of AHPP, the effective antihypertensive amount is 100-9000 mg/day/adult patient. See column 2, lines 63-65. It is also taught that uric acid

production was inhibited by AHPP in a dose dependant manner. See column 4, Example 5.

Maeda et al. do not explicitly teach the administration of a therapeutically effective amount of xanthine oxidase inhibitor to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality. See page 670, left hand column bottom paragraph-right hand column, line 9. It is also taught that hypertensive people with serum uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

It would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such effective amounts of xanthine oxidase inhibitor needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl, because 1) Maeda et al. teaches that uric acid production was inhibited by xanthine oxidase inhibitor, AHPP in a dose dependent manner, and 2) the optimization of amounts of known agents to be administered to achieve a desired effect, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. One of ordinary skill in the art at the time of invention would have been motivated to optimize the amount of xanthine oxidase inhibitor with reasonable expectation of obtaining uric acid levels of 5.0-6.9 mg/dL in treating hypertension because Ward teaches that hypertension is associated with serum uric acid levels, and uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

Furthermore, it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955.) Maeda et al. also exemplifies that uric acid production was inhibited by AHPP in a dose dependent manner.

Response to Arguments

Applicant's arguments have been fully considered, but not found persuasive as discussed below.

Maeda et al. teaches a method of treating hypertension by administering a xanthine oxidase inhibitor, AHPP in an amount of 100-9000 mg/day. It is also taught that the uric acid production was inhibited by AHPP, i.e AHPP has the property of reducing uric acid levels when administered to a patient in the method of treating hypertension. Accordingly, it would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such as effective amounts of xanthine oxidase inhibitor needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl, because Maeda et al. teaches administration of AHPP in the method of treating hypertension, and also teaches that uric acid production was inhibited by xanthine oxidase inhibitor, AHPP in a dose dependent manner. Further, the optimization of amounts of known agents to be administered to achieve a desired effect, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. Thus, the methods as taught by Maeda et al. necessarily result in reducing uric acid levels as recited in the claims, when the

amounts of AHPP to be administered are modified or optimized to achieve desired therapeutic effects i.e treat hypertension effectively. Note that applicant acknowledges that uric acid was known as a possible risk factor for hypertension, and Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality.

Further, it is pointed out that xanthine oxidase inhibitor, inhibits the conversion of xanthine to uric acid i.e xanthine oxidase inhibitor when employed for treating hypertension reduces uric acid levels in the patient. Maeda et al. also exemplifies that uric acid production was inhibited by xanthine oxidase inhibitor AHPP in a dose dependent manner. Thus, the methods as taught by Maeda et al. necessarily result in reducing uric acid levels as recited in the claims, when the amount of AHPP are modified to achieve desired therapeutic effects.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baldwin et al. (4,032,522, PTO-892), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892).

Baldwin et al. discloses a method of reducing uric acid in a patient by administering xanthine oxidase inhibitors, trifluoromethylimidazoles. See abstract; column 2. It is also disclosed that the compounds therein are anti-hyperuricemic agents, and exhibit anti-hypertensive activity. See column 5, lines 36-45; column 6, lines 5-52. The compounds therein are administered in an amount of 100-800 mg per day. See column 11, lines 50-54.

Baldwin et al. do not specifically teach the administration of a therapeutically effective amount of xanthine oxidase inhibitor to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality. See page 670, left hand column bottom paragraph-right hand column, line 9. It is also taught that hypertensive people with serum uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

It would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such effective amounts of xanthine oxidase inhibitor needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl, since the optimization of amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. One of ordinary skill in the art at the time of invention would have reasonably expected to treat hypertension by modifying the effective amounts of xanthine oxidase inhibitor to achieve desired uric acid levels because Ward teaches that hypertension is associated with serum uric acid levels.

Furthermore, it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955.)

Response to Arguments

Applicant's arguments have been fully considered, but not found persuasive. Baldwin et al. teaches a method of reducing uric acid in a patient by administering xanthine oxidase inhibitors, trifluoromethylimidazoles, and also teaches that the compounds therein are anti-hyperuricemic agents, and exhibit anti-hypertensive activity. Accordingly, it would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such effective amounts of xanthine oxidase inhibitor needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl, since the optimization of amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. One of ordinary skill in the art at the time of invention would have reasonably expected to treat hypertension by modifying the effective amounts of xanthine oxidase inhibitor to achieve desired therapeutic effect. Thus, the methods as taught by Baldwin et al. necessarily result in reducing uric acid levels as recited in the claims, when the amounts of xanthine oxidase inhibitor are modified to achieve desired therapeutic effects i.e treat hypertension effectively. Note that applicant acknowledges that uric acid was known as a possible risk factor for hypertension, and

Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality.

Further, it is pointed out that xanthine oxidase inhibitor, inhibits the conversion of xanthine to uric acid i.e xanthine oxidase inhibitor when employed for treating hypertension reduces uric acid levels in the patient. Thus, the methods as taught by Baldwin et al. necessarily result in reducing uric acid levels as recited in the claims, when the amount of xanthine oxidase inhibitors, trifluoromethylimidazoles are modified to achieve desired therapeutic effects.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamoto et al. (EP 0 337 350, PTO-1449), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892).

Nakamoto et al. discloses a method of lowering uric acid comprising administering a xanthine oxidase inhibitor, allopurinol. See page 2, lines 15-20. It is also disclosed that compounds that reduce uric acid are effective in curing hypertension. See page 6, lines 1-2.

Nakamoto et al. do not specifically teach the administration of a therapeutically effective amount of allopurinol to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality. See page 670, left hand column bottom paragraph-right hand column, line 9. It is also taught that hypertensive people with serum uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer allopurinol to treat hypertension.

One of ordinary skill in the art at the time of invention would have been motivated to administer allopurinol with reasonable expectation of success of treating hypertension by lowering uric acid because Nakamoto teaches that uric acid lowering agents are known to treat hypertension.

It would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such effective amounts needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl because Ward teaches that uric acid is a risk factor for hypertension, and uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke. Thus, one of ordinary skill in the art at the time of invention would have been motivated to optimize the effective amounts of allopurinol with reasonable success of lowering uric acid to desired levels to treat hypertension.

Response to Arguments

Applicant argues that "Nakamoto does not even teach the mechanism by which dimethylheptylphenyl butanoyl ethanolamine compound works. It does not appear to even be a xanthine oxidase inhibitor. For fairness sake, it cannot be reasonably said that this one confusing statement concerning an unknown compound can suggest the use of a xanthine oxidase inhibitor to treat hypertension." This argument has been considered, but not found persuasive because Nakamoto's reference was employed for its teaching that allopurinol is known to lower uric acid, and also teaches that compounds that lower uric acid are effective in treating hypertension. Nakamoto teaches that allopurinol is a well known uric acid lowering agent, and also teaches that compounds that lower uric acid are effective in treating hypertension. Accordingly, one of ordinary skill in the art would have been motivated to administer, uric acid lowering agent, allopurinol with reasonable expectation of treating hypertension. Further, opitimization of result effective parameters such as amounts of ingredients to obtain desired therapeutic effects is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamoto et al. (EP 0 337 350, PTO-1449).

Nakamoto et al. discloses a method of lowering uric acid comprising administering a xanthine oxidase inhibitor, allopurinol. See page 2, lines 15-20. It is also disclosed that compounds that reduce uric acid are effective in curing hypertension. See page 6, lines 1-2.

Nakamoto et al. do not explicitly teach the employment of allopurinol in the method of treating hypertension.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer allopurinol in the method of treating hypertension because Nakamoto et al. teach that compounds that reduce uric acid are effective in curing hypertension. Accordingly, one of ordinary skill in the art at the time of invention would have been motivated to administer uric acid lowering agent, allopurinol with reasonable expectation of success of treating hypertension.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Tuesday-Thursday, 7.30 am-3.30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617

S. Wang
SHENGJUN WANG
PRIMARY EXAMINER